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Fusion of Fish and Man

By Joshua Lederberg

THE ARCAINE subject of cell biology has recently undergone a quiet revolution that will undoubtedly exert a profound influence on human affairs in keeping with its impact on experimental science. This is the manipulation of pure cultures of tissue cells by somatic hybridization, a method of causing different cells to fuse with one another.

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That this sometimes occurred in the body of the normal animal had been suspected for a long time. The first demonstration that tissue cells not only fuse but that the result is a new, viable hybrid line of cells is credited to Drs. G. Barski, S. Sorieul and F. Cornefert of the Cancer Institute of Paris, work first reported in 1960. Their compatriot at the University of Paris, Prof. Boris Ephrussi, gave this work important impetus as a tool for studies of cell genetics.

The discovery by Japanese and British researchers that certain viruses would promote cell fusion has made the technique a reproducible one, especially with the help of viruses that have been inactivated by ultraviolet light so as not to interfere in other ways with the development of the hybrid cells.

THE EXPERIMENTAL results have been outstanding, almost bizarre. The fusion of cells is frequently followed by a fusion of their nuclei, with an intermixing of the chromosomes. The hybrid nucleus continues to propagate regularly as such in succeeding cell divisions.

As a rule, then, hybrid cells are mixed both for the nucleus and the cytoplasm of the parent cells. However, as shown by Prof. Henry Harris of the Pathology Department of Oxford University, when nucleated red blood cells are used, these cells burst, leaving naked nuclei which then fuse with the other cells. This result allows a clear separation of the information carried in the cell by the nucleus and the cytoplasm, respectively.

The most remarkable finding, perhaps, is that cells from very different animal species can fuse. Thus it has been possible to prepare hybrid cells obtained by somatic combinations as widely separated as fish and man. Since other known processes can lead to the loss of various chromosomes, a vast new field of experimental genetics is opened. It is now feasible to synthesize cell lines which have most or all of their genes from one species with a single chromosome or part of a chromosome from another.

THE USUAL reproductive process of animals is, of course, very narrowly species-limited. We pay special attention to rare exceptions like the mule, a donkey-horse hybrid. This restriction has been a serious one for experimental genetics, making it impossible to analyze the very important differences between remote species, for example, between man and the apes.

Human genetics has also been impeded by the obvious difficulties of achieving the experimental matings that might be the most revealing tests of gene effects. It is now possible to bypass these restrictions. While we do not yet make entire hybrid organisms, many fundamental aspects of cell genetics and biochemistry become amenable to experimental study. Important findings are begin-

ning to emerge whose details will doubtless inspire many further reports and commentaries.

FOR THE moment passing over these, and some of the more strident futuristic implications of somatic hybridization, we should note some of the easier practical applications that are bound to emerge. Genetic or immunological individuality is now the most vexing barrier to replacing incompetent tissues by transplantation. Somatic hybrid cells would be of advantage in medicine if they combined the immunological individuality of the recipient cells with the biochemical capabilities of the donor.

The immunological individuality would insure that the cells remained acceptable to the host. The biochemical capabilities could then be imported for specialized functions like replenishing a hormone, say, to treat diabetes, or to recognize and destroy aberrant cells, an approach to a treatment for cancer.

In all likelihood, however, the fundamental knowledge uncovered by these techniques will far exceed any of the simple-minded applications we now have the imagination to foresee.

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